

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING
OF A CHANGE(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

GILL JENNINGS & EVERY
Broadgate House
7 Eldon Street
London EC2M 7LH
ROYAUME-UNI

| | |
|--|---|
| Date of mailing (day/month/year) 17 October 2001 (17.10.01) | IMPORTANT NOTIFICATION |
| Applicant's or agent's file reference REP05969WO | |
| International application No. PCT/GB99/04376 | |
| | International filing date (day/month/year) 22 December 1999 (22.12.99) |

1. The following indications appeared on record concerning:

☒ the applicant ☒ the inventor ☐ the agent ☐ the common representative

| | | |
|---|----------------------------|--------------------------|
| Name and Address SANTANGELO, Joseph, David Dept. of Infectious Diseases Imperial College School of Medicine at the Hammersmith Campus Du Cane Road London W12 0NN United Kingdom | State of Nationality GB | State of Residence GB |
| | Telephone No. | |
| | Facsimile No. | |
| | Teleprinter No. | |

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☐ the person ☐ the name ☐ the address ☒ the nationality ☐ the residence

| | | |
|---|----------------------------|--------------------------|
| Name and Address SANTANGELO, Joseph, David Microscience Limited 545 Eskdale Road Winnersh Triangle Wokingham Berkshire RG41 5TU United Kingdom | State of Nationality US | State of Residence GB |
| | Telephone No. | |
| | Facsimile No. | |
| | Teleprinter No. | |

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

| | |
|---|---|
| <input checked="" type="checkbox"/> the receiving Office | <input type="checkbox"/> the designated Offices concerned |
| <input type="checkbox"/> the International Searching Authority | <input checked="" type="checkbox"/> the elected Offices concerned |
| <input checked="" type="checkbox"/> the International Preliminary Examining Authority | <input type="checkbox"/> other: |

| | |
|---|--|
| The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland | Authorized officer Maria Victoria CORTIELLO |
| Facsimile No.: (41-22) 740.14.35 | Telephone No.: (41-22) 338.83.38 |

PATENT COOPERATION TREATY

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NOTIFICATION OF THE RECORDING
OF A CHANGE(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

GILL JENNINGS & EVERY
Broadgate House
7 Eldon Street
London EC2M 7LH
ROYAUME-UNI

Date of mailing (day/month/year)

25 July 2001 (25.07.01)

Applicant's or agent's file reference

REP05969WO

IMPORTANT NOTIFICATION

International application No.

PCT/GB99/04376

International filing date (day/month/year)

22 December 1999 (22.12.99)

1. The following indications appeared on record concerning:

☒

the applicant

☒

the inventor

☐

the agent

☐

the common representative

Name and Address

HENWOOD, Caroline, Joanne
140 Gurney Court Road
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Hertfordshire AL1 4RJ
United Kingdom

State of Nationality

GB

State of Residence

GB

Telephone No.

Facsimile No.

Teleprinter No.

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☐

the person

☐

the name

☒

the address

☐

the nationality

☐

the residence

Name and Address

HENWOOD, Caroline, Joanne
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AL4 9TW
United Kingdom

State of Nationality

GB

State of Residence

GB

Telephone No.

Facsimile No.

Teleprinter No.

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

☒

the receiving Office

☐

the International Searching Authority

☒

the International Preliminary Examining Authority

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the designated Offices concerned

☒

the elected Offices concerned

☐

other:

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Maria Victoria CORTIELLO

Telephone No.: (41-22) 338.83.38

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PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents
United States Patent and Trademark
Office
Box PCT
Washington, D.C.20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

| | |
|--|--|
| Date of mailing (day/month/year) 10 August 2000 (10.08.00) | Applicant's or agent's file reference REP05969WO |
| International application No. PCT/GB99/04376 | Priority date (day/month/year) 22 December 1998 (22.12.98) |
| International filing date (day/month/year) 22 December 1999 (22.12.99) | Priority date (day/month/year) 22 December 1998 (22.12.98) |
| Applicant HUGHES, Martin, John, Glenton et al | |

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

03 July 2000 (03.07.00)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

| | |
|--|---|
| The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35 | Authorized officer S. Mafla Telephone No.: (41-22) 338.83.38 |
|--|---|

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WORLD INTELLECTUAL PROPERTY ORGANIZATION
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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

| | | | | | | | | | | | | | | | | | | | | | |
|---|------------------------------|----|--|-----------|-----------------------------|----|-----------|----------------------------|----|-----------|----------------------------|----|-----------|--------------------------|----|-----------|------------------------|----|-----------|------------------------------|----|
| (51) International Patent Classification ⁷ : C07K 14/00 | | A2 | (11) International Publication Number: WO 00/37490 | | | | | | | | | | | | | | | | | | |
| | | | (43) International Publication Date: 29 June 2000 (29.06.00) | | | | | | | | | | | | | | | | | | |
| (21) International Application Number: PCT/GB99/04376 | | | <p>mersmith Campus, Du Cane Road, London W12 0NN (GB). FELDMAN, Robert [GB/GB]; Dept. of Infectious Diseases, Imperial College School of Medicine at the Hammersmith Campus, Du Cane Road, London W12 0NN (GB). MOORE, Joanne, Christine [GB/GB]; Dept. of Infectious Diseases, Imperial College School of Medicine at the Hammersmith Campus, Du Cane Road, London W12 0NN (GB). EVEREST, Paul [GB/GB]; Dept. of Infectious Diseases, Imperial College School of Medicine at the Hammersmith Campus, Du Cane Road, London W12 0NN (GB). DOBSON, Richard, James [GB/GB]; Dept. of Infectious Diseases, Imperial College School of Medicine at the Hammersmith Campus, Du Cane Road, London W12 0NN (GB). HENWOOD, Caroline, Joanne [GB/GB]; 140 Gurney Court Road, St. Albans, Hertfordshire AL1 4RJ (GB). DOUGAN, Gordon [GB/GB]; ICSTM, Dept. of Biochemistry, Exhibition Road, London SW7 2AZ (GB). WILSON, Rebecca, Kerry [GB/GB]; ICSTM, Dept. of Biochemistry, Exhibition Road, London SW7 2AZ (GB).</p> <p>(74) Agent: GILL JENNINGS & EVERY; Broadgate House, 7 Eldon Street, London EC2M 7LH (GB).</p> <p>(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).</p> <p>Published Without international search report and to be republished upon receipt of that report.</p> | | | | | | | | | | | | | | | | | | |
| (22) International Filing Date: 22 December 1999 (22.12.99) | | | | | | | | | | | | | | | | | | | | | |
| (30) Priority Data: | | | | | | | | | | | | | | | | | | | | | |
| <table><tr><td>9828346.8</td><td>22 December 1998 (22.12.98)</td><td>GB</td></tr><tr><td>9901233.8</td><td>20 January 1999 (20.01.99)</td><td>GB</td></tr><tr><td>9901234.6</td><td>20 January 1999 (20.01.99)</td><td>GB</td></tr><tr><td>9908321.4</td><td>12 April 1999 (12.04.99)</td><td>GB</td></tr><tr><td>9912036.2</td><td>24 May 1999 (24.05.99)</td><td>GB</td></tr><tr><td>9922596.3</td><td>23 September 1999 (23.09.99)</td><td>GB</td></tr></table> | | | | 9828346.8 | 22 December 1998 (22.12.98) | GB | 9901233.8 | 20 January 1999 (20.01.99) | GB | 9901234.6 | 20 January 1999 (20.01.99) | GB | 9908321.4 | 12 April 1999 (12.04.99) | GB | 9912036.2 | 24 May 1999 (24.05.99) | GB | 9922596.3 | 23 September 1999 (23.09.99) | GB |
| 9828346.8 | 22 December 1998 (22.12.98) | GB | | | | | | | | | | | | | | | | | | | |
| 9901233.8 | 20 January 1999 (20.01.99) | GB | | | | | | | | | | | | | | | | | | | |
| 9901234.6 | 20 January 1999 (20.01.99) | GB | | | | | | | | | | | | | | | | | | | |
| 9908321.4 | 12 April 1999 (12.04.99) | GB | | | | | | | | | | | | | | | | | | | |
| 9912036.2 | 24 May 1999 (24.05.99) | GB | | | | | | | | | | | | | | | | | | | |
| 9922596.3 | 23 September 1999 (23.09.99) | GB | | | | | | | | | | | | | | | | | | | |
| (71) Applicant (for all designated States except US): MICROSCIENCE LIMITED [GB/GB]; 12 St. James's Square, London SW1Y 4RB (GB). | | | | | | | | | | | | | | | | | | | | | |
| (72) Inventors; and | | | | | | | | | | | | | | | | | | | | | |
| (75) Inventors/Applicants (for US only): HUGHES, Martin, John, Glenton [GB/GB]; Dept. of Infectious Diseases, Imperial College School of Medicine at the Hammersmith Campus, Du Cane Road, London W12 0NN (GB). SANTANGELO, Joseph, David [GB/GB]; Dept. of Infectious Diseases, Imperial College School of Medicine at the Hammersmith Campus, Du Cane Road, London W12 0NN (GB). LANE, Jonathan, Douglas [GB/GB]; Dept. of Infectious Diseases, Imperial College School of Medicine at the Ham- | | | | | | | | | | | | | | | | | | | | | |
| (54) Title: OUTER SURFACE PROTEINS, THEIR GENES, AND THEIR USE | | | | | | | | | | | | | | | | | | | | | |
| (57) Abstract | | | | | | | | | | | | | | | | | | | | | |
| <p>According to the present invention, a series of genes are identified in Group B <i>Streptococcus</i>, the products of which may be located on the outer surface of the organism. The genes, or functional fragments thereof, may be useful in the preparation of therapeutics, e.g. vaccines for the immunisation of a patient against microbial infection.</p> | | | | | | | | | | | | | | | | | | | | | |

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

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| CU | Cuba | LC | Saint Lucia | RU | Russian Federation | | |
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| DK | Denmark | LR | Liberia | SG | Singapore | | |
| EE | Estonia | | | | | | |

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
29 June 2000 (29.06.2000)

PCT

(10) International Publication Number
WO 00/37490 A3

(51) International Patent Classification⁷: **C12N 15/53**,
15/54, 15/55, 15/61, 15/62, 9/02, 9/10, 9/12, 9/22, 9/92,
C07K 14/315, 16/12, A61K 38/44, 38/45, 38/46

(21) International Application Number: PCT/GB99/04376

(22) International Filing Date:
22 December 1999 (22.12.1999)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
9828346.8 22 December 1998 (22.12.1998) GB
9901233.8 20 January 1999 (20.01.1999) GB
9901234.6 20 January 1999 (20.01.1999) GB
9908321.4 12 April 1999 (12.04.1999) GB
9912036.2 24 May 1999 (24.05.1999) GB
9922596.3 23 September 1999 (23.09.1999) GB

(71) Applicant (for all designated States except US): **MICRO-SCIENCE LIMITED** [GB/GB]; 12 St. James's Square, London SW1Y 4RB (GB).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **HUGHES, Martin, John, Glenton** [GB/GB]; Microscience Limited, 545 Eskdale Road Winnersh Triangle, Wokingham, Berkshire RG41 5TU (GB). **SANTANGELO, Joseph, David** [US/GB]; Microscience Limited, 545 Eskdale Road, Winnersh Triangle, Wokingham, Berkshire RG41 5TU (GB). **LANE, Jonathan, Douglas** [GB/GB]; Microscience Limited, 545 Eskdale Road Winnersh Triangle, Wokingham, Berkshire RG41 5TU (GB). **FELDMAN, Robert** [GB/GB]; Microscience Limited, 545 Eskdale Road Winnersh Triangle, Wokingham, Berkshire RG41 5TU (GB). **MOORE, Joanne, Christine** [GB/GB]; Microscience Limited, 545 Eskdale Road Winnersh Triangle,

Wokingham, Berkshire RG41 5TU (GB). **EVEREST, Paul** [GB/GB]; 16 Redclyffe Gardens, Helensburgh Dumbartonshire, G84 9JJ (GB). **DOBSON, Richard, James** [GB/GB]; Microscience Limited, 545 Eskdale Road Winnersh Triangle, Wokingham, Berkshire RG41 5TU (GB). **HENWOOD, Caroline, Joanne** [GB/GB]; 16 Portman Close, St. Albans, Hertfordshire, AL4 9TW (GB). **DOUGAN, Gordon** [GB/GB]; ICSTM, Dept. of Biochemistry, Exhibition Road, London SW7 2AZ (GB). **WILSON, Rebecca, Kerry** [GB/GB]; 5 Mornington Avenue, West Kensington, London W14 8UJ (GB).

(74) Agent: **GILL JENNINGS & EVERY**; Broadgate House, 7 Eldon Street, London EC2M 7LH (GB).

(81) Designated States (*national*): AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:

— with international search report

(88) Date of publication of the international search report:
20 September 2001

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: OUTER SURFACE PROTEINS, THEIR GENES, AND THEIR USE

(57) Abstract: According to the present invention, a series of genes are identified in Group B *Streptococcus*, the products of which may be located on the outer surface of the organism. The genes, or functional fragments thereof, may be useful in the preparation of therapeutics, e.g. vaccines for the immunisation of a patient against microbial infection.

WO 00/37490 A3

ENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

| | | |
|--|---|--|
| Applicant's or agent's file reference REP06969W0 | FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below. | |
| International application No. PCT/GB 99/ 04376 | International filing date (day/month/year) 22/12/1999 | (Earliest) Priority Date (day/month/year) 22/12/1998 |
| Applicant MICROSCIENCE LIMITED et al. | | |

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 6 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☒ contained in the international application in written form.

☒ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☒ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☐ None of the figures.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB 99/04376

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-12 (all partially)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-12 (all partially)

A peptide encoded by the gene MS4, obtainable from Group B Streptococcus, or a homologue thereof or a functional fragment thereof, preferably said peptide comprising the amino acid sequence of SEQ ID NO:2, preferably for therapeutic use. A polynucleotide encoding said peptide (SEQ ID NO:1), a host cell expressing said peptide, a vaccine comprising said peptide, and an antibody against said peptide. Use of said peptide, said polynucleotide or said host cell for screening potential drugs, for the detection of virulence, or for the manufacture of a medicament for use in the treatment or prevention of a bacterial infection, e.g. of a Group B Streptococcal infection, preferably a focal or a urinary tract infection.

2. Claims: 1-12 (all partially)

As invention 1 but concerning a peptide encoded by the gene MS10, preferably comprising the amino acid sequence of SEQ ID NO:12, and a polynucleotide encoding said peptide (SEQ ID NO:11).

3. Claims: 1-12 (all partially)

As invention 1 but concerning a peptide encoded by the gene MS11, preferably comprising the amino acid sequence of SEQ ID NO:4, and a polynucleotide encoding said peptide (SEQ ID NO:3).

4. Claims: 1-12 (all partially)

As invention 1 but concerning a peptide encoded by the gene MS14, preferably comprising the amino acid sequence of SEQ ID NO:10, and a polynucleotide encoding said peptide (SEQ ID NO:9).

5. Claims: 1-12 (all partially)

As invention 1 but concerning a peptide encoded by the gene MS16, preferably comprising the amino acid sequence of SEQ ID NOs:6 and 8, and a polynucleotide encoding said peptide (SEQ ID NOs:5 and 7).

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/GB 99/04376

A. CLASSIFICATION OF SUBJECT MATTER

| | | | | | |
|-------|------------|-----------|-----------|-----------|-----------|
| IPC 7 | C12N15/53 | C12N15/54 | C12N15/55 | C12N15/61 | C12N15/62 |
| | C12N9/02 | C12N9/10 | C12N9/12 | C12N9/22 | C12N9/92 |
| | C07K14/315 | C07K16/12 | A61K38/44 | A61K38/45 | A61K38/46 |

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C07K A61K G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, STRAND, MEDLINE, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category ° | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|--|-----------------------|
| A | WO 98 23631 A (KNOWLES DAVID JUSTIN CHARLES ; LONETTO MICHAEL ARTHUR (GB); SMITHKL) 4 June 1998 (1998-06-04) Note: 78.9% nt seq identity of SEQ ID NO:1 (rev strand) with seq id #3864296 (nt 944-1961) in 1018 bp overlap, 87.1% aa seq identity of SEQ ID NO:2 with translated ORF in 224 aa overlap. page 89-90 | 1-8,12 |
| A | EP 0 230 777 A (SUMITOMO CHEMICAL CO ; SUMITOMO PHARMA (JP); OHGEN RESEARCH LAB LTD) 5 August 1987 (1987-08-05) Note: 87.5% nt seq identity with SEQ ID NO:1 in 321 bp overlap. figure 2 | 1-5 |

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

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Date of the actual completion of the international search

15 May 2000

Date of mailing of the international search report

22.03.01

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
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van de Kamp, M

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 99/04376

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K38/52 A61K39/09 G01N33/53

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|---|-----------------------|
| P,A | EP 0 913 476 A (SMITHKLINE BEECHAM CORP) 6 May 1999 (1999-05-06) Note: 79.0% nt seq identity of SEQ ID NO:1 with SEQ ID NO:1 in 1017 bp overlap, 88.9% aa seq identity of SEQ ID NO:2 with SEQ ID NO:2 in 334 aa overlap. the whole document | 1-8,12 |
| A | --- LARSSON C ET AL.: "Experimental vaccination against Group B Streptococcus, an encapsulated bacterium, with highly purified preparations of cell surface proteins Rib and alpha" INFECTION AND IMMUNITY, vol. 64, no. 9, September 1996 (1996-09), pages 3518-3523, XP002135397 abstract --- -/-- | 1-12 |

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

° Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

15 May 2000

Date of mailing of the international search report

22.03.01

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International Application No

PCT/GB 99/04376

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category ° | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|--|-----------------------|
| A | WO 94 21685 A (LINDAHL GUNNAR ;STAALHAMMAR CARLEMALM MARGARET (SE); STENBERG LARS) 29 September 1994 (1994-09-29) page 2, line 11-16 examples 1-8 --- | 1-12 |
| A | WO 94 10317 A (GEN HOSPITAL CORP ;BRIGHAM & WOMENS HOSPITAL (US)) 11 May 1994 (1994-05-11) page 66, line 28 -page 67, line 1 examples 1-15 page 4, line 1 -page 5, line 11 --- | 1-12 |
| A | TRICOT C ET AL.: "Evolutionary relationships among bacterial carbamoyltransferases" JOURNAL OF GENERAL MICROBIOLOGY, vol. 135, no. 9, September 1989 (1989-09), pages 2453-2464, XP000856002 abstract ----- | 1-8,12 |

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 99/04376

| Patent document cited in search report | | Publication date | Patent family member(s) | Publication date |
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| WO 9823631 | A | 04-06-1998 | EP 1023311 A | 02-08-2000 |
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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

| | | |
|---|---|--|
| Applicant's or agent's file reference REP05969WO | FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) | |
| International application No. PCT/GB99/04376 | International filing date (day/month/year) 22/12/1999 | Priority date (day/month/year) 22/12/1998 |
| International Patent Classification (IPC) or national classification and IPC C07K14/00 | | |
| Applicant MICROSCIENCE LIMITED et al. | | |

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 9 sheets, including this cover sheet.

- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☒ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☒ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☒ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

| | |
|---|--|
| Date of submission of the demand 03/07/2000 | Date of completion of this report 10.05.2001 |
| Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465 | Authorized officer Roscoe, R Telephone No. +49 89 2399 2554  |

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB99/04376

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1-10 as originally filed

Claims, No.:

1-12 as originally filed

Sequence listing part of the description, pages:

1-19, as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☒ contained in the international application in written form.
- ☒ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB99/04376

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

II. Priority

1. ☐ This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:

☐ copy of the earlier application whose priority has been claimed.

☐ translation of the earlier application whose priority has been claimed.

2. ☐ This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid.

Thus for the purposes of this report, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:
see separate sheet

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 1-12(all part).

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 1, 3-12(all part) are so unclear that no meaningful opinion could be formed (*specify*):
see separate sheet

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 1-12(all part).

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB99/04376

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

- ☐ the written form has not been furnished or does not comply with the standard.
☐ the computer readable form has not been furnished or does not comply with the standard.

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

- ☐ restricted the claims.
☐ paid additional fees.
☐ paid additional fees under protest.
☐ neither restricted nor paid additional fees.

2. ☒ This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

- ☐ complied with.
☒ not complied with for the following reasons:
see separate sheet

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

- ☐ all parts.
☒ the parts relating to claims Nos. 1-12(all part).

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

| | | | |
|-------------------------------|------|--------|-----------|
| Novelty (N) | Yes: | Claims | 1-12 |
| | No: | Claims | |
| Inventive step (IS) | Yes: | Claims | |
| | No: | Claims | 1-12 |
| Industrial applicability (IA) | Yes: | Claims | 1-6, 8-12 |
| | No: | Claims | 7 |

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB99/04376

2. Citations and explanations
see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB99/04376

II. Priority

Two relevant (to MS4) priority documents exist. GB98283446.8 (22.12.98) discloses a partial amino acid sequence of MS4 (82 aa) and the corresponding nucleic acid sequence. The sequence shows one discrepancy to the complete MS4 sequence provided in the second priority document (GB9922596.3 (23.09.99)) which appears to match the sequence in the filed application. Since the MS4 sequence is claimed in the same context in the priority documents and the application, priority will be valid insofar as the sequence disclosures are entitled to priority. Hence, the second priority document establishes valid priority for all of the claims. The first document however provides a short and partially incorrect (1 aa) sequence. Specific sequences are only entitled to priority when they are actually disclosed in the priority document. The sequences in the application document thus differ from the first priority document, are more extensive and are defined (in terms of broadening) in a different manner. Hence, none of the claims are considered entitled to priority from 22.12.98.

As a result, D3 (EP0913476) is relevant prior art in the International Phase.

III. No Opinion

No opinion can presently be expressed for the peptide of claim 1 insofar as said peptide relates to functional fragments or homologues since the scope of these items is unclear. The same applies to the subject-matter in claims 3-12 that relates thereto. It is noted that homologs of MS4 with high levels of sequence identity up to 90% at protein level (values given together with citations in search report) are known from a number of species, and are further used (as well as fragments thereof) in Streptococcal vaccine preparations (D1-D3 and D7). When applicant drafts acceptably clear claims he will need to avoid overlap with these disclosures.

Further, no opinion is expressed for the claims insofar as they extend beyond the content of invention group I. See section IV.

IV. Lack of Unity

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB99/04376

Five invention groups were identified in the International Search Report. Applicant only paid for invention group I to be searched (claims 1-12 (all part) insofar as relate to gene MS4). Hence, examination has to be similarly restricted. Objection based on lack of structural and functional features shared between claimed peptides and fact that cell-surface-exposed gene products of Group B streptococcus are per se known to the skilled person.

V. Reasoned statement on Novelty, Inventive Step and Industrial Applicability

The documents mentioned in the present written opinion / International Preliminary Examination Report are numbered as in the search report, i.e. D1 corresponds to the first document of the search report etc.

- Novelty (Art.33(2) PCT)

No objections are raised specifically to the MS4 protein of Seq.ID No.2 and the corresponding DNA. Same applies to rest of claims insofar as they specifically relate thereto (see also section III).

- Inventive Step (Art.33(3) PCT)

The prior art (D1 or D3 which could each be taken as closest prior art) discloses sequences of homologous ornithine carbamoyltransferase (OCT) (MS4) genes with around 79% sequence identity to the present gene. These applications further refer to the isolation of similar sequences by e.g. hybridization technology. Applicant has merely identified a similar sequence from another Streptococcus sp. This is considered to be trivial, since surface-exposed proteins such as ornithine carbamoyltransferases (which are clearly not highly species specific virulence factors - see any detailed bacteriology textbook i.e. are known to be widespread among the Streptococci - no Streptococci lacking such an enzyme is known to the IPEA) would be of interest for vaccination strategies and if considered useful therefore in one Streptococcal species (D1 and D3) would be expected to be similarly useful in another. Applicant has thus merely selected to isolate OCT as one of a number of potentially useful antigens he could have isolated from Group B streptococci by looking for homologs of equivalent antigens that have been

isolated in e.g. *S. pneumoniae*. This is considered to be a non-inventive selection which is not accompanied by any surprising effect. Hence, the present claims are considered to lack inventive step.

- **Industrial Applicability (Art.33(4) PCT)**

For the assessment of the present claims 7 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Claims 7 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

VI. **Certain documents**

In accordance with Rule 70.10, PCT, applicants attention is drawn to the following document(s):

D3: EP-A-0913476 (Publication date, 06.05.99; Priority date, 30.10.97; Filing date, 22.10.98)

VIII. **Certain observations**

- **Clarity (Art.6 PCT)**

Terminology MS4 is arbitrary denomination which must be replaced or supplemented by a technical definition.

A peptide encoded by an operon including a certain gene is clearly totally

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB99/04376

undefined as any gene could be inserted into a synthetic operon and thus any peptide could be meant. Further, not all members of the natural operon from the source used by applicant are specifically listed - hence these can not be considered.

The terminology "homologue" and "functional" needs to be clarified in claim 1. In particular, the level of sequence identity of the homolog needs to be specified as does the function of the fragment.

The antibody of claim 12 needs to be defined as specifically binding to a specific sequence, i.e. not just binding to a sequence defined in a partially open-ended manner. Presently the claim is also worded in an unacceptable product-by-process manner.